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COMMON cold

One sure sign of winter's approach—and an unwelcome occurrence other times of the year as well—is the common cold. Though a mild illness, it is one which has so far defied most efforts at control or cure.

The Symptoms

Headache, sneezing, stuffy nose, sore throat, a general feeling of fatigue—these are the symptoms of the common cold. Temperatures usually do not increase more than one degree in adults or go to higher than 102° in children. The disease normally runs its course in two to seven days. Regardless of the time of year, if "colds" occur frequently, or last much longer than a week, they may not be colds at all, but allergies or sinus infections. Coughs, particularly if prolonged, may also indicate more serious infections.

The Health Cost

The National Center for Health Statistics has estimated that in 1976 more than 96 million colds occurred in the United States, accounting for 20% of all acute illnesses. These colds resulted in some 276 million days of restricted activity, a loss of 30 million school days and 30 million work days. Other estimates of the annual incidence indicate an average of eight colds per year for children under four years of age and two colds per year for adults for a total of as many as one billion colds per year. In any case, statistics do not adequately reflect the toll in reduced vitality, decreased efficiency and below-standard productivity. The dollar cost of respiratory pharmaceuticals—pills and formulas for promised relief of runny or stuffed-up noses—is estimated at more than $550 million per year.

The Cause

More than 100 different viruses can cause a "common cold"; but in studies of colds only one-third to one-half of the infections can be related to a specific virus. In the others, no agent can be isolated.

The rhinoviruses were the first important group of viruses to be associated with colds in adults and are the major known cause. These agents cause 25 to 30% of all infections. A new group, the "coronaviruses", has recently emerged as a possible important cause of adult colds occurring from December through February—a period when rhinoviruses are uncommon.

There are other viruses which may cause "common cold" symptoms in some people but in most victims are associated with more serious illnesses. These are the myxoviruses (which include the influenza and other viruses), the paramyxoviruses, the adenoviruses, and the enteroviruses.

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"Catching" A Cold

Direct contact with a person who has a cold is the best way to "catch" the disease. Rhinoviruses are transmitted in nasal and throat secretions of the infected person. It has long been thought that this transmission took place primarily through sneezes or coughs which spray the viruses into the air where they hang, ready to be inhaled by someone in the same car, at the same table, or at the next desk.

Now, grantees of the National Institute of Allergy and Infectious Diseases (NIAID) have reported that other instruments of transmission may be the hands. The University of Virginia scientists found that, under natural conditions, rhinoviruses can be transmitted from an infected person's hands to an intermediary surface, such as a table, or directly to the fingers of a healthy recipient. Infection in the susceptible person then results from self-inoculation of virus on the finger onto the mucous membranes of the eye or nose.

Other NIAID grantees at the University of Wisconsin have indicated that cold viruses may not be as easily transmitted from one person to another as previously thought; but, rather, a fairly simple mechanical device, such as viricidal tissue, may help break the chain of rhinovirus transmission. These researchers found that the major factors involved in the transmission of cold-causing viruses are the time spent in the presence of a person with a cold, the severity of his or her symptoms and the amount of virus shed.

Epidemiology

The same University of Virginia grantees who had researched rhinovirus transmission conducted a study on a group of office workers in Charlottesville, Virginia which showed that participants had an average of two and one-half colds per year, with one rhinovirus cold every other year. There was an abrupt increase in acute respiratory diseases beginning in September and continuing through mid-October each year.

Almost half of the total sick-leave taken by the office workers was due to acute respiratory diseases. The study also showed that among adults—at least in Charlottesville—colds occur most frequently in those living with children. Another finding of this study was that rhinoviruses caused a relatively small proportion of colds suffered by children, although during the September-October "outbreaks" the incidence of rhinovirus colds is about the same for children as for adults.

Another epidemiologic study carried out in a Michigan community showed that infants under one year of age had the most colds, averaging six a year. In children under three years of age, boys had more colds than girls. In all later years, females suffered most frequently from an upper respiratory infection.

The most surprising finding from this NIAID-supported study was that more colds were reported to start on Monday than on any other day of the week. This observation was particularly true in the school age population, leading the investigators to theorize that cold viruses are usually transmitted at school or work during the week, with cold symptoms gradually developing over the week-end and reaching their peak on Mondays.

Identification of Viruses

Through efforts of NIAID scientists and other virologists around the world, over 100 distinct rhinovirus types have been identified. The coordination of a vast collaborative program, aimed at defining the number of rhinovirus serotypes, has been the responsibility of NIAID's Laboratory of Infectious Diseases, which is designated by the World Health Organization as an International Reference Center for Respiratory Diseases Other Than Influenza.

In an effort to accelerate and facilitate common cold studies, NIAID contractors have prepared 89 seed rhinoviruses and antisera. These research materials, which are made available to scientists on request, are expected to identify over 75% of isolates obtained from common cold sufferers.

The coronaviruses were first recovered by scientists in England. Thus far, 32 coronavirus strains have been described, 16 of these by NIAID scientists.

One difficulty encountered in isolating and identifying a coronavirus is the problem of growing these organisms. Certain coronavirus strains seem to prefer organ cultures to tissue culture cell monolayers, the laboratory technique usually used for growing viruses. Organ cultures consist of small amounts of human fetal trachea or nasal mucosa in which the virus is grown in petri dishes in the laboratory. This technique was first used in England and later at the NIAID laboratories to grow certain of the viruses that were subsequently grouped under the term coronavirus.

Preventing or Treating Colds

Factors affecting susceptibility to the common cold are also under study. One NIAID research team, for example, has investigated a popular belief concerning the cause of a cold. Using volunteer subjects, the scientists found that chilling, exposure, or overheating apparently has little effect on the development of or seriousness of a cold. If a rhinovirus infects the body, a cold usually develops, and the importance of other factors has not been demonstrated.

Although many non-prescription cold remedies can be purchased, the claims of most of these to prevent or relieve cold symptoms cannot be substantiated, according to a study carried out by the National Academy of Sciences.

A recent Consumer Report from the Food and Drug Administration (FDA) makes it clear that, although nonprescription drugs can be effective in relieving symptoms associated with colds, these products will not prevent, cure or even shorten the course of the common cold. This same report also indicates that many of the current labeling and advertising claims of over-the-counter cold products are misleading and may have to be changed, or the products themselves reformulated, in order to comply with proposed new FDA standards for acceptable ingredients and labeling claims for cough, cold, and related remedies.

It has recently been reported by NIAID grantees that use of aspirin in treating colds increases the amount of virus shed in nasal secretions and, thus, makes the cold sufferer more of a hazard to others. However, the Illinois investigators who made this discovery believe that, though people should be made aware of this potential for increased transmission, the choice of taking aspirin for cold should be left up to the individual patient and his doctor.

Many people are convinced that taking substantial quantities of ascorbic acid, or Vitamin C, will prevent colds or diminish the severity and duration of symptoms. To test this theory, several large-scale, controlled studies of both children and adults have been conducted.

To date, scientists are generally agreed that results of these studies do not show that large doses of Vitamin C prevent colds. There is some indication that the vitamin may reduce the severity or duration of symptoms but conclusive evidence is lacking. Moreover, it has been noted that taking Vitamin C over long periods of time in the large amounts recommended may actually constitute a health hazard. Too much ascorbic acid can cause diarrhea, a danger for elderly people and small children. Excessive Vitamin C also causes the body to form oxalic acid, an ingredient in some kidney stones. And, finally, the acidifying effect of Vitamin C on the urine could render misleading the urine tests for sugar and could interfere with the treatment of diabetes.

Antiviral Research

A promising area of research on treatment relates to the stimulation of antiviral activity in the body. Antiviral agents are substances that, in various ways, inhibit the ability of a virus to replicate in cells.

One antiviral substance that is being intensively studied at the NIAID is inter-

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feron, a part of the body's natural defense system. Interferon is generally species-specific (for example, mouse interferon is most effective in mouse cells and human interferon in human cells), but not virus-specific. It should be particularly useful, therefore, in treating an infection such as the common cold, which can be caused by so many different viruses.

An NIAID-supported scientist at Stanford University reported in 1973 that, by using relatively large doses of human interferon, he could prevent colds in human volunteers. However, the cost of producing human interferon outside the human body—in cell cultures—is so high, at present, that its use is prohibitive under ordinary circumstances.

More recently, scientists at the University of Illinois have found that a drug known as propanediamine, if administered immediately after exposure to cold-causing virus, seems to reduce cold symptoms and virus shedding. The NIAID grantees also found that the effectiveness of the drug could be linked to its ability to induce high levels of interferon. Although these results are encouraging, they have not been reproduced by other investigators.

At present, the NIAID has in progress a collaborative antiviral research program which includes efforts to increase in the host, the amounts of interferon produced, and to prepare human interferon outside the body. This program is also evaluating a number of other products for antiviral activity. These include calcium eleonolate, Ribavarin, and Tilarone. Information on these chemicals is still sketchy but one day they—or compounds like them—may take their place as effective antidotes for the common cold.

The Outlook

Although scientists have attempted to develop a vaccine against the viruses causing the common cold, several problems exist. Early in the study of colds it was suggested that a "cocktail" vaccine be developed against the main rhinoviruses. However, the great number of virus types and the absence of any one common factor has made the possibility of producing such a combination vaccine extremely unlikely.

Scientists interested in developing a vaccine have studied the most effective way to administer such a preparation. The information they have provided may also have application for future antiviral drugs. Two types of neutralizing antibodies or immunoglobulins—IgG and IgA—are important in studies on the prevention of the common cold. Both of these are found in the blood serum, but IgA is found in greater abundance in tears, intestinal and respiratory tract secretions, and in mammary gland fluid.

According to NIAID scientists, secretory IgA may be the clue to effective control of the common cold. Using an inactivated rhinovirus 13 vaccine administered intramuscularly, scientists, in one study, showed that a high level of serum antibody (mainly IgG) was produced, but that the individuals, when exposed to live rhinovirus 13, still became ill. However, when the vaccine was administered intranasally via nose drops, both nasal and serum antibody levels increased, and a significant number of the vaccinated individuals resisted experimental infection. Thus, since the first site of infection in the common cold is the nose, it may be the appropriate site in which to induce sufficient levels of secretory antibody or interferon to fight the virus.

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